UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/638,648	08/14/2000	David M. Stern	0575/62097/JPW/JML	9845

7590 02/12/2003

John P White
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, NY 10036

EXAMINER	
TON, THAIAN N	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 02/12/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/638,648	STERN ET AL.	
	Examiner	Art Unit	
	Thai-An N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4 and 7-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4 and 7-16* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' Amendment, filed 10/30/02, Paper No. 12, has been entered.

Claims 5 and 6 have been cancelled. Claim 1 has been amended.

Claims 1, 2, 4, 7-16 are under current examination.

Any rejection made of record in the prior Office action, mailed 4/24/02, Paper No. 11, and not made of record in the instant Office action, has been withdrawn in view of Applicants amendments to the claims.

Claim Objections

Claim 1 is objected to because of the following informalities: The term, "vasoconstriction" is misspelled. See line 2 of the claim.. Appropriate correction is required.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

The prior rejection of claims 1-11 and 16 under 35 U.S.C. 101 is withdrawn. The prior rejection of claims 12-15 which are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 12-15 of copending Application No. 09/992,955 is maintained. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. Applicants request that the Examiner continue to hold the rejection in abeyance. Applicants point out that subject to this application being otherwise allowable, and copending application serial No. 09/992,955 being allowed, Applicants would consider filing a Terminal Disclaimer. It is noted, as *supra*, that the filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 4, 7-11 and 16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over

claims 1, 2-11 and 16 of copending Application No. 09/992,995. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to methods for decreasing cerebral vasoconstriction in a subjection suffering from an Alzheimer's disease-type pathology which comprises administering to the subject an inhibitor of RAGE and methods for treatment of Alzheimer's disease in a subject by administration of an inhibitor of RAGE are obvious over the claims of the '995 Application, which are directed to methods of decreasing cerebral vasoconstriction in a subject suffering from amyloid angiopathy by administration of an inhibitor of RAGE, and methods for the treatment of amyloid angiopathy by administration of an inhibitor of RAGE. In particular, the instant claims directed to methods of treatment for subjects suffering from an Alzheimer's disease-type pathology is encompassed by cerebral amyloid angiopathy, as evidencd by claims 4-5 of the '995 Application which states that amyloid angiopathy is due to Alzheimer's disease.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior rejection of claims 1, 2, 4, 7-16 under 35 U.S.C. 112, first paragraph, is maintained because the specification, while being enabling for methods of decreasing cerebral vasoconstriction and ameliorating neurovascular stress in a transgenic *mouse* which over expresses mutant human amyloid beta precursor protein (APP), bearing the double mutation Lys670Asn and Met 671Leu, (TG APP sw +/- mice) by administration of a soluble receptor for advanced glycation endproduct (sRAGE), the specification does not reasonably provide enablement for methods of decreasing cerebral vasoconstriction, ameliorating neurovascular stress or treatment of Alzheimer's disease in *all* transgenic non-human animal subjects or human subject by administration of *any* inhibitor of RAGE. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants argue that it would not have required undue experimentation to carry out the claimed invention. Applicants contend that the Examiner has failed to provide any evidence that would rebut the applicants' reasonable correlation between the disclosed *in vivo* utility of the present claims and the *in vivo* animal model data recited in the specification. Applicants directed the Examiner to MPEP §2163 and contend that the Examiner has failed to present any evidence rebutting the disclosure of the present invention. Applicants point the Examiner to the disclosure which recites that the treatment of cerebral vasoconstriction in the Hsaio

mouse model of the present invention is "powerful in terms of its implications since the mice are considered a model of Alzheimer's disease-type pathology." Applicants argue that the Examiner fails to provide any evidence to rebut this fact. See p. 10, ¶ 2-3 of the Response.

Applicants further contend that the *in vivo* administration of sRAGE to Hsaio mice, a model of Alzheimer's-type pathology, inhibited Aβ induced cerebral vasoconstriction, an Alzheimer's-type pathology in humans. Applicants contend that based upon the use of an art-accepted murine model of an AD-type pathology in a human, the relevant evidence as a whole demonstrates a reasonable correlation between the disclosed *in vivo* utility of the present claims and the *in vivo* animal model data recited in the specification. Accordingly, Applicants conclude that it would not have required undue experimentation to carry out the claimed invention. See p. 11, ¶ 1-2 of the Response.

Applicants' arguments have been considered, however, they are not found persuasive. In particular, the claimed invention, as broadly written, reads on any subject(s), which are, administered an inhibitor of RAGE. The term "subjects" encompasses any subjects, including transgenic non-human animals. The claims have not been limited to the exemplified TG APP sw +/- mice, or any transgenic mice, and as such, the prior rejection, with regard to the state of the art of transgenic non-human animals is maintained for reasons of record advanced on pages 5-11 of the prior Office action. Furthermore, it is maintained that the

specification fails to teach methods of decreasing cerebral vasoconstriction and amelioration of neurovascular stress in any other transgenic non-human animal, including any other transgenic mice, other than the exemplified TG APP sw +/- mice.

The specification does not provide guidance or teaching to overcome the unpredictabilities associated with the art of transgenesis, and as such, it would have required undue experimentation for one of skill in the art to predict the results achieved in any particular subject [including any transgenic mouse or a human subject]. The state of the art of transgenics is such that although one of skill would be able to produce a transgenic mouse with a transgene of interest, however, the art is not predictable with regard to the transgene behavior and the resulting phenotype [see the prior Office action, pp. 8-9]. In the instant case, the described TG APP sw +/- have a particular phenotype that is dependent upon a particular transgene. This is further supported by Ali *et al.* [**Neurobio. Of Aging**, 17:223-234, 1996], who teach the generation of transgenic mice modeling Alzheimer-type amyloidgenesis, and find that changes in APP in the brains of the transgenic mice was due to mouse stran-specific artifacts. In particular, Ali state that the mouse strain selected for generating transgenic animals is a critically important variable, and that putative pathological changes must be scrutinized to avoid misleading interpretations. Further, that, "In conjunction with reports of partially successful models of AD pathology and Aβ-mediated cell death, it is clear that much more

information is needed to enable the routine development of a reliable animal model for the full range of AD-type pathology." [See p. 232, 2nd column, last paragraph]. Accordingly, it is reiterated that the state of the art of transgenesis is such that it would not be unpredictable with regard to transgene behavior and the resulting phenotype.

Accordingly, in view of the lack of guidance and direction in the specification for the use of sRAGE to decrease cerebral vasoconstriction or ameliorate neurovascular stress in any other species other than TG APP sw +/- mice, the lack of guidance or teaching for the treatment of an Alzheimer's disease-type pathology in any subject, and the unpredictable state of the art with of transgenesis and the resulting phenotype, it would have required undue experimentation for one skilled in the art to carry out the claimed methods, animals and use thereof.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thái-An N. Ton whose telephone number is (703) 305-1019. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the examiner be unavailable, inquiries should be directed to Deborah Reynolds, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-4051. Any administrative or procedural questions should be directed to William Phillips, Patent Analyst, at (703) 305-3482. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

TNT

Thái-An N. Ton
Patent Examiner
Group 1632

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP 1800/1630